

REMARKS

New Amendments

In addition to the amendments presented in the June 29, 2006 Rule 116 Reply, claims 1 and 2 are amended above to change the term "heteroarylalkyl" in the definition of R^3 to heterocycle-alkyl and change "heteroaryl portion" to heterocyclic portion. This is consistent with the original language which indicated that the heteroarylalkyl could be partially or fully saturated.

Also, claims 13, 14, 18, and 19 are amended to correct a typographical error. In original claim 1, heteroaryl was not included in the description of R^3 , whereas heteroarylalkyl was included. Thus, claims 13, 14, 18, and 19 should recite a heteroarylalkyl group for R^3 . The claims are amended to change pyridyl to pyridylmethyl in the definition of R^3 . See the exemplified compounds recited in claim 6 in which R^3 is pyridylmethyl.

These amendments do not require further search and/or consideration and, moreover, place the application in condition for allowance. Entry thereof is respectfully requested.

Advisory Action issued July 14, 2006

In the Advisory Action issued July 14, 2006, entry of the amendments filed June 29, 2006 was denied on grounds that the change from Beghet's disease to Behcet's disease was not the correction of an obvious typographical error, and thus constituted new matter. Applicants respectfully disagree.

Applicants made this correction after an Examiner handling a different application (Serial No. 10/636,996; Office Action of March 17, 2006) noted the typographical error and suggested the correction. Also, attached is an excerpt from Dorland's Illustrated Medical Dictionary, 26th Edition (1981), which at page 161 lists "Behcet's syndrome (disease)," but does not list any condition called Beghet's disease. Further, a search of issued patents, using the PTO's data base, did not reveal any patents that mentioned "Beghet's disease." Thus, it is respectfully submitted that one of ordinary skill in the art

would have recognized that Beghet's disease was a typographical error, and that Behcet's disease was intended. Entry of the amendments is therefore respectfully requested.

The following are the arguments and remarks presented in the prior Rule 116 Reply filed June 29, 2006.

Allowed Subject Matter

Applicants gratefully acknowledge the Examiner's indication that claims 1-9, 13, 14, 16-26, 28, 36-47, and 52 are allowed.

Amendments

Claim 49 and page 33 of the specification are amended to correct an obvious typographical error.

Claims 29, 30, 34, 35, 48, 50, 51, and 53-55 are cancelled by the above amendments. Thus, the only claims pending that are not already allowed are claims 33 and 49. Applicants reserve the right to file a divisional application directed to the cancelled subject matter.

Claim 33 is amended to recite a method of treating a patient suffering from inflammation, rather than treating a patient suffering from an allergic or inflammatory disease. Claim 49 depends from claim 33 and specifies what diseases/conditions have induced the inflammation.

New claims 56-57 depend from claim 49 and are directed to the treatment of inflammation due to specific conditions/diseases recited in claim 49.

Rejection under 35 USC 112, first paragraph

Claims 20, 30, 33-35, 48-51, and 53-55 are rejected as allegedly being non-enabled. This rejection is respectfully traversed.

Initially, it should be noted that the inclusion of claim 20 is assumed to be a typographical error. Instead, it appears that claim 29 was intended. For example, the "Office Action Summary" indicates that claim 20 is allowed and that claim 29 is rejected.

As noted above, claims 29, 30, 34, 35, 48, 50, 51, and 53-55 are cancelled. Thus, the only pending claims that are rejected are claims 33 and 49.

In the rejection, it is acknowledged that applicants' disclosure is enabling for "a method for enhancing cognition and a method for the treatment of inflammation and inflammation due to asthma and chronic obstructive pulmonary disease." Claim 33 is amended to recite a method of treating a patient that is suffering from inflammation. Thus, the rejection acknowledges that claim 33, as amended, is enabled. Claim 49 and new claims 56-57 depend from claim 33 and thus also are enabled. Therefore, withdrawal of the rejection is respectfully requested.

In any event, applicants disagree with the assertion of nonenablement with respect to the cancelled claims. Method claims are inherently functional. In other words, the literal scope of the method claims encompass only those embodiments that achieve the specified function. See, e.g., *In re Angstadt*, 190 USPQ 214 (CCPA 1976) and *Dinn-Nguyen et al.*, 181 USPQ 46 (CCPA 1974).

Applicants' specification clearly discloses that the compounds in question are PDE4 inhibitors. The specification also discloses that these PDE4 inhibitors can be used to treat diseases and conditions for which PDE4 inhibitors are known in the art to have activity. No reason is presented in the rejection to doubt the veracity of these statements in applicants' disclosure. Furthermore, the disclosure provides more than adequate guidance for one of ordinary skill in the art to determine the relative amount of PDE4 activity for any given compound within the claimed methods using no more than routine experimentation.

An application disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken in compliance with the enablement requirement of the first paragraph 35 U.S.C. § 112, unless there is reason to doubt the objective truth of statements contained therein relied on for enabling support. *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995). *Fiers v. Revel*, 984 F.2d 1164, 24 USPQ2d 1601 (Fed. Cir. 1993). Furthermore, as stated in *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (CCPA 1971), the PTO must have adequate support for its challenge to the credibility of applicant's statements of enablement. See also *In re Bundy*, 209 USPQ 48 (CPA 1981).

As discussed above, the rejection does not provide reasons to doubt the veracity of statements in applicants' disclosure that the compounds possess PDE4 inhibitory activity. Further, the art recognizes that compounds possessing PDE4 inhibitory activity can be used to treat the diseases and/or conditions recited in the claims.

To establish the requisite objective enablement under the 35 USC 112, first paragraph, an applicants' disclosure is not required to present specific test results such as *in vivo* or *in vitro* test results. All that is required under the statute is **objective** enablement. See, e.g., *In re Marzocchi et al.*, at 369:

The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

The MPEP is also in agreement with the holding in *Marzocchi*. The MPEP states that “compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed.” See MPEP § 2164.02.

The test for enablement is not whether any experimentation is needed but whether or not that experimentation is undue. See, *In re Angstadt*, 190 USPQ 214, 219 (CCPA 1976) in which the art involved (catalysis) was acknowledged to be unpredictable. Even a considerable amount of experimentation, or complex experimentation, is permissible if it is routine. See, e.g., *Ex parte Jackson*, 217 USPQ 804, 807 (POBA 1982) and *In re Wands*, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988).

Merely because it is alleged that a specific example of treating a disease is not presented in the specification, one of ordinary skill in the art would not doubt the truth of the statements concerning the activity of the compounds. As noted above, MPEP § 2164.02 states that compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. The nature of the invention and the state of the art, as discussed above, further demonstrate that applicants' specification provides sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention.

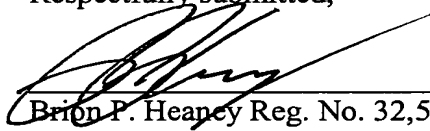
With respect to guidance, applicants' specification provides more than sufficient guidance with respect to dosages, formulations, modes of administration, and assays for determining the relative amount of PDE4 inhibitory activity.

In view of the above remarks, it is respectfully submitted that applicants' disclosure provides more than sufficient guidance to objectively enable one of ordinary skill in the art to make and use the claimed invention with no more than routine experimentation. The rejection does not present sufficient reasons to doubt the veracity of the enablement statements set forth in the disclosure.

In view of the above remarks, allowance of the instant application is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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Attorney Docket No.: MEMORY-29

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DORLAND'S ILLUSTRATED

Medical Dictionary

Twenty-sixth Edition

1981

W. B. SAUNDERS COMPANY Philadelphia London Toronto
Mexico City Sydney Tokyo

being surmounted by a cradle covered with gauze. **capillary b.**, the total combined mass of capillaries forming a large reservoir which may be more or less completely filled with blood. **circoelectric b.**, trademark for a revolving circular bed which induces constant pressure alteration. **ether b.**, a bed made up to facilitate the transfer of an unconscious patient from an operating table or stretcher to the bed. **fracture b.**, a bed for the use of patients with broken bones. **Gatch b.**, a bed fitted with joints beneath the hips and knees of the patient, allowing him to be raised to a half-sitting position and be so maintained by elevating his knees to prevent his sliding toward the footboard. **hydrostatic b.**, a water bed. **Klondike b.**, a bed arranged for outdoor sleeping so that the patient is protected from draughts. **metabolic b.**, a bed so arranged that all the feces and urine of the patient are saved; the amount of excreta compared with the intake gives an indication of the metabolism in the body. **nail b.**, the modified area of epidermis beneath the nail, over which the nail plate slides forward as it grows; called also *matrix unguis* [NA]. **Sanders b.**, a powered, rocking bed, used in the treatment of chronic occlusive arterial disease to improve circulation. **sawdust b.**, a bed made from sawdust which is used to prevent bed sores. **Vickers hyperbaric b.**, a small portable unit for administering hyperbaric oxygen therapy, particularly in myocardial infarction; its maximum pressure is 2 atmospheres. **water b.**, a rubber mattress filled with water; used to prevent bed sores by evenly distributing the patient's weight; called also *Arnott's b.*

bedbug (bed'bug) a bug of the family Cimicidae, genus *Cimex*. *C. lectularius*, of temperate regions, and *C. rotundatus* (*hemipterus*), of the tropics, are flattened, oval, reddish insects which inhabit houses, furniture and neglected beds and feed on man, usually at night.

bedfast (bed'fast) unable to leave the bed.

bedlam (bed'lam) [*Bedlam*, the Bethlehem Royal Hospital, London, a mental hospital established in 1402] 1. an institution for patients with mental illness. 2. bedlamism.

bedlamism (bed'lam-izm) a state of wild tumult; bedlam.

Bednar's aphtha (bed'narz) [Alois *Bednar*, physician in Vienna, 1816-1888] see under *aphtha*.

bedpan (bed'pan) a vessel for receiving the urinary and fecal discharges of a patient unable to leave his bed.

Bedsonia (bed-so'ne-ah) *Chlamydia*.

bedsore (bed-sor) decubitus ulcer.

beef (bēf) the meat of an adult bull, steer, ox, or cow. **b., iron, and wine**, a preparation of beef extract, ferric ammonium citrate, and other ingredients in sherry wine; formerly used as a hematinic agent.

beer (bēr) the fermented infusion of malted barley and hops.

Beer's collyrium, knife, operation (ba'erz) [Georg Joseph *Beer*, German ophthalmologist, 1763-1821] see under *collyrium, knife, and operation*.

beerwort (bēr'wert) an infusion of malt in water intended to be converted into beer; it is sometimes used for the cultivation of yeasts and molds.

beeswax (bēz'waks) wax derived from the honeycomb of *Apis mellifera*; see *yellow wax*, under *wax*. **bleached b.**, see *white wax*, under *wax*. **unbleached b.**, see *yellow wax*, under *wax*.

Beevor's sign (bē'vorz) [Charles Edward *Beevor*, British neurologist, 1854-1908] see under *sign*.

Begbie's disease (beg'bēz) [James *Begbie*, Scottish physician, 1798-1869] Graves' disease.

Beggiatoa (bej'je-ah-to'ah) [named for F. S. *Beggiato*] a genus of microorganisms, order Beggiatoales, family Beggiatoaceae.

Beggiatoaceae (bej'je-ah-to-a'se-e) a family of Schizomycetes (order Beggiatoales), made up of cells which are generally not visible without staining, arranged in chains within trichomes which show flexing motion and also show gliding movements when in contact with a substrate. It includes four genera, *Beggiatoa*, *Thioploca*, *Thiospirillopsis*, and *Thiothrix*. These are free-living sulfur bacteria, often found in association with blue-green algae.

Beggiatoales (bej'je-ah-to-a'lēz) a taxonomic order of class Schizomycetes, made up of cells which occur singly, or in motile or nonmotile trichomes, and which multiply by transverse fission. They are found in fresh or salt water, and in soil and decomposing organic material, especially algae. It includes four families, Achromatiaceae, Beggiatoaceae, Leukotrichaceae, and Vitreoscillaceae.

begma (beg'mah) [Gr. *bēgma* phlegm] 1. a cough. 2. the material evacuated from the lungs by coughing (sputum).

behavior (be-hāv'yor) deportment or conduct; any or all of a person's total activity, especially that which can be externally observed. **automatic b.**, automatism, def. 1. **invariable b.**, activity whose character is determined by innate structure, such as reflex action. **operant b.**, see under *conditioning*. **protean b.**, an irregular, unpredictable sequence of movements by prey when pursued by predators. **respondent b.**, see *conditioning*. **variable b.**, behavior that is modifiable by individual experience.

behaviorism (be-hāv'yor-izm) a school of psychology based upon a purely objective observation and analysis of human and animal behavior without reference to the testimony of consciousness.

behaviorist (be-hāv'yor-ist) a psychologist who is a disciple of behaviorism.

Behçet's syndrome (disease) (ba'sets) [Hulusi *Behçet*, dermatologist, Istanbul, Turkey, 1889-1948] see under *syndrome*.

Béhiér-Hardy sign (symptom) (ba'he-a har'de) [Louis Jules *Béhiér*, French physician, 1813-1876; Louis Philippe Alfred *Hardy*, French physician, 1811-1893] see under *sign*.

Behla's bodies (ba'lahs) [Robert Franz *Behla*, German physician, 1850-1921] Plimmer's bodies.

Behring's law, tuberculin (ba'ringz) [Emil Adolph von *Behring*, German bacteriologist, 1854-1917; winner of the Nobel prize for medicine in 1901] see under *law*, and see *tuberculosis and tulose*.

BEI butanol-extractable iodine.

Beigel's disease (bi'gelz) [Hermann *Beigel*, German physician, 1830-1879] piedra.

beikost (bi'kōst) [Ger.] solid and semisolid baby foods, i.e., those other than milk or formula feedings.

bejel (bej'el) nonvenereal syphilis (q.v.) occurring in Africa, the Middle East, the Balkans, Central Asia, and Africa.

Békésy (bek'ē-se), Georg von. Hungarian-born physicist, born 1899; winner of the Nobel prize in medicine and physiology for 1961, for his discoveries concerning the physical mechanisms of stimulation within the cochlea.

Bekhterev's (Bechterew's) arthritis, etc. (bek-ter'yevs) [Vladimir Mikhailovich *Bekhterev*, Russian neurologist, 1857-1927] see under *arthritis, disease, layer, nucleus, reaction, reflex, symptom, and tests*.

Bekhterev-Mendel reflex (bek-ter'yev-men'del) [V. M. *Bekhterev*; Kurt *Mendel*, German neurologist, 1857-1927] Mendel-Bekhterev reflex.

bel (bel) the common logarithm of the ratio of two powers, usually electric or acoustic powers; such ratios are usually expressed in decibels (q.v.). An increase of one bel in intensity approximately doubles the loudness of most sounds.

Belascaris (bē-las'kah-ris) *Toxocara*. **B. ca'ti**, *Toxocara cati*. **B. margina'ta**, *Toxocara canis*. **B. mys'tax**, *Toxocara cati*.

belching (belch'ing) eructation; the noisy voiding of gas from the stomach through the mouth.

belemnoid (be-lem'noid) [Gr. *belemnōn* dart + *eidos* form] 1. dart-shaped. 2. the styloid process of the ulna or of the temporal bone.

Belfield's operation (bel'fēldz) [William Thomas *Belfield*, surgeon in Chicago, 1856-1929] vasotomy.

Bell's law, nerve, palsy (paralysis), phenomenon [Sir Charles *Bell*, Scottish physiologist in London, 1774-1842] see *nervus thoracicus longus*, and see under *law, palsy, and phenomenon*.

Bell's mania (disease) [Luther Vose *Bell*, American physician, 1806-1862] see under *mania*.

Bell's muscle [John *Bell*, Scottish surgeon and anatomist, 1763-1820] see under *muscle*.

Bell's treatment [William Blair *Bell*, British gynecologist, 1871-1936] see under *treatment*.

Bell-Magendie law (bel'ma-jen'de) [Sir Charles *Bell*; François *Magendie*, French physiologist, 1783-1855] Bell's law.

belladonna (bel'ah-don'ah) [Ital. "fair lady"] the *Atrapa belladonna* L. (Solanaceae), or deadly nightshade, a perennial plant indigenous to central and southern Europe and cultivated in North America, containing various anticholinergic alkaloids (e.g., atropine, hyoscyamine, belladonnine, scopolamine, etc.), some of which are produced during the extraction process. Called also *banewort*, *death's herb*, and *dwale*. *Belladonna leaf* [USP], consisting of the dried leaves and fruiting tops of *A. belladonna* or *A. belladonna* var. *acuminata*, is used in the preparation of standardized dosage forms; see under *extract and tincture*. The root has also been used.

belladonnine (bel'ah-don'nēn) chemical name: 1,2,3,4-tetrahydro-1-phenyl-1,4-naphthalenedicarboxylic acid bis(8-methyl-8-azobicyclo[3.2.1]oct-3-yl)ester. An alkaloid, C₂₄H₂₄N₂O₄, derived from belladonna and related solanaceous plants, produced during the process of extraction.

bellaradine (bel-ar'ah-din) cuscohygrine.

bell-crowned (bel-krownd') having a crown somewhat bell-shaped; said of a tooth that is larger than usual at the occlusal measurement and that tapers toward the neck, or cervix.

Bellini's ducts (tubules), ligament (bel-e'nēz) [Lorenzo *Bellini*, Italian anatomist, 1643-1704] see *tubuli renales recti*, and see under *ligament*.

Belloq's cannula (sound, tube) (bel-oks') [Jean Jacques *Belloq*, French surgeon, 1732-1807] see under *cannula*.

belly (bel'e) 1. the abdomen. 2. the fleshy, contractile part of a muscle; called also *venter musculi* [NA]. **anterior b. of di-**